Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 23-29, 31, 33-39, 41, 43-51, 53, 55-64, 66, 68-77, 79, 81-83, 84-89, 91, 93-97 and 99 are pending and under consideration in the application, with 23, 33, 43, 55, 68, 81 and 93 being the independent claims in this group. Claims 30, 32, 40, 42, 52, 54, 65, 67, 78, 80, 90, 92, 98, 100-114, 115, and 116 were withdrawn from consideration. Claim 82 is sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Claims 35, 47, 60, 73, and 83 have been amended. Support for these amendments can be found in the specification, *inter alia*, at page 15, third full paragraph and page 23, second full paragraph. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicant(s) respectfully request(s) that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Objection to the Specification

The Examiner stated that the priority information on page 1 of the specification must be amended to indicate that Parent Application 08/852,824 is now U.S. Patent No. 6,060,272 and issued on May 9, 2000. Applicants have amended the specification accordingly.

The Examiner stated that on page 4 of the specification, Applicant has written "Brief Explanation of the Accompanying Drawings". Applicant respectfully disagrees. On page 5 the title "Brief Description of the Figures" is used to describe the figures.

The Examiner stated that the specification does not indicate the address of where clone 209004 was deposited. The specification has been amended to reflect the correct address for the ATCC and deposit information. Additionally, as stated below in response to the enablement rejection, a statement concerning ATCC Deposit 209003 will be submitted upon receipt by the undersigned.

Accordingly, withdrawal of these objections are respectfully requested.

Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 35, 47, 60, 73, 82, 83, 93, 94-97 and 99 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Paper No. 8, page 4.)

The Examiner has stated that claim 93 "is indefinite because it is not clear which amino acids comprise the transmembrane domain of SEQ ID NO:2 so as to allow the metes and bounds of the claims to be determined." (Paper No. 8, page 4.) Claims 94-97 and 99 depend from claim 93. Applicants respectfully disagree with the Examiner's rejection.

The specification teaches that the transmembrane regions of G-protein coupled receptors, such as EBI-2, are generally designated as TM1-TM7 and that each transmembrane region constitutes a stretch of 20-30 hydrophobic amino acids (page 2, line 32, page 3, lines 9-10). Since the amino acid sequence of EBI-2 is provided (SEQ ID

NO:2), one skilled in the art can easily evaluate this sequence and identify the hydrophobic amino acid stretches. An amino acid sequence comparison of EBI-2 (SEQ ID NO:2) and EBI-1 (SEQ ID NO:17), another G- protein coupled receptor, is also provided (*See* Specification, Figure 2). The transmembrane domains of EBI-1 were known (*See* Schweickart *et al.*, attached hereto). One of ordinary skill would understand which amino acids comprise the transmembrane regions of EBI-2.

As discussed at pages 2-3 of the specification, G-protein coupled receptors have a well-characterized and distinctive structural topology that is found in all members of the superfamily. In particular, several references report the manual and computer-aided alignment of hundreds of G-protein coupled receptors. *See, e.g.*, Probst *et al., DNA and Cell Biology 11*:1-20 (1992) (manual alignment of 74 unique human G-protein coupled receptors); and Oliveira, L. *et al., J. Computer-Aided Mol. Design 7*:649-658 (1993) (visual alignment of approximately 100 receptors and computer-aided alignment of 225 receptors). This structural homology further confirms the metes and bounds of the transmembrane regions of SEQ ID NO: 2. Therefore, claim 93 is definite, and Applicants respectfully request that the Examiner withdraw the rejection.

The Examiner states that claims 35, 47, 60, and 73 are indefinite "because it is unclear what 'activity' the G-protein coupled receptor has" and that "the 'activity' of the G-protein coupled receptor has not been disclosed in the claims nor the specification." (Paper No. 8, page 4.) Applicants have amended claims 35, 47, 60, and 73 by deleting the offending term "activity." Accordingly, the Examiner is respectfully requested to withdraw the rejection.

The Examiner states that claim 82 and dependent claim 83 are indefinite "because it is unclear what is the mature polypeptide." (Paper No. 8, page 4.) Applicants have canceled

claim 82, and have amended claim 83 to depend from claim 81. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

Claim Rejections under 35 U.S.C. § 101

Claims 23-29, 31, 33-39, 41, 43-51, 53, 55-64, 66, 68-77, 79, 81-89, 91, 93-97 and 99 were rejected under 35 U.S.C. § 101 for allegedly not being supported by either a specific, substantial utility or a well established utility.

I. The Examiner Has Failed to Establish That An Artisan of Ordinary Skill Would Reasonably Doubt All Asserted Utilities.

Applicants note that the manner of making and using an invention disclosed in a specification must be accepted by the PTO "unless there is reason to doubt the objective truth of the statements contained therein." *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971); *see also Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1098-99 (Jan. 5, 2001) ("*Utility Guidelines*"). Instances in which an assertion of specific utility is not credible are rare. *See* MPEP § 2107 (7th ed. Rev. 1, Feb. 2000). Indeed, the Federal Circuit recently affirmed the standard for making a utility rejection that was set forth in *In re Brana*, 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995):

> The PTO cannot make this type of rejection . . . unless it has reason to doubt the objective truth of the statements contained in the written description. *See Brana*, 51 F.3d at 1566, 34 USPQ2d at 1441.

In re Cortright, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999). The PTO's own guidelines

provide:

> Any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility. Whenever possible, the examiner should provide documentary evidence . . . (e.g., scientific or technical journals, excerpts from treatises or books, or U.S. or foreign patents) to support the factual basis for the prima facie showing of no specific and substantial credible utility. If documentary evidence is not available, the examiner should specifically explain the scientific basis for his or her factual conclusions.

Utility Guidelines, 66 Fed. Reg. at 1098. Further, the Federal Circuit has recently articulated the standard for utility:

> The threshold of utility is not high: An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 (1996); *Brooktree Corp. v. Advanced Micro Devices*, Inc., 977 F.2d 1555, 1571 (Fed. Cir. 1992) ("To violate § 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is capable of serving any beneficial end").

Juicy Whip, Inc. v. Orange Bang Inc., 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999).

The Examiner has not made the required showing that even one, much less all, of the disclosed utilities for the G-protein coupled receptor polynucleotides would be unbelievable in light of the teachings of the specification -- under either the standard set forth in *Juicy Whip* or the PTO's guidelines. The specification discloses that monoclonal antibodies raised against EBI-2 may be useful as therapeutics for heart disease, atherosclerosis, and restenosis. (*See* original specification, page 8, line 19.) In addition, the specification discloses that EBI-2 polynucleotide probes or antibodies may be used to

for the detection of EBI-2 expression in vein endothelial cells. (*See* original specification, page 15, third full paragraph.) Finally, the specification discloses that GPCR antagonists have been used for the treatment of angina pectoris and myocardial infarction (paragraph spanning pages 22-23) and that GPCR agonists are useful for the treatment of acute heart failure and hypotension (page 23, lines 4-5). Thus, the polynucleotides of the claims can be used for the diagnosis of heart disease, including myocardial infarction. For example, a polynucleotide sequence that is 90% identical to 150 contiguous nucleotides of SEQ ID NO: 1 as recited in claims 23 and 26 will hybridize to EBI-2 polynucleotides and be useful for detecting heart disease. Therefore, the claimed polynucleotides certainly provide some identifiable benefit under *Juicy Whip*, and their utility is specific and substantial under the PTO's guidelines.

Thus, the Examiner has failed to provide any evidence or sound scientific reasoning to establish that an artisan would reasonably doubt all of the asserted utilities for the polynucleotides of the claims.

II. The Specification Discloses At Least One Specific Utility.

Applicants respectfully emphasize that the specification does disclose at least one specific activity of the EBI-2 G-protein coupled receptor. Moreover, it is apparent that the instant case is not analogous to the situation in *Brenner v. Manson*, contrary to the Examiner's implication. (Paper No. 8, page 13.)

In *Brenner*, the issue was not whether a disclosed utility was sufficient. Rather, the applicant was trying to establish an earlier date of invention for the purpose of provoking an interference. 383 U.S. at 521. Indeed, the examiner's initial basis for

refusing to declare an interference was that the applicant had *failed to disclose any utility* at all. *Id.* at 521. Thus, the issue in *Brenner* was whether the applicant had made an adequate "showing" to establish a prior date of invention, i.e., whether "the process claim has been reduced to production of a product shown to be useful" through actual demonstration of the utility. *Id.* at 534. The only evidence offered by the applicant to make this showing was a reference to an article by a third party showing the activity of an adjacent homologue of the subject steroid compound. *See id.* at 521-522. The appellate court agreed that the applicant had done nothing to show or demonstrate that the compound was indeed useful. *See id.* at 521. Thus, it upheld the rejection of the request for declaration of an interference. *Id.* at 536.

In contrast, the issue in the present case is whether the instant application explicitly teaches at least one utility that meets the requirements of § 101. Applicants submit that the specification discloses a number of specific uses for EBI-2 G-protein coupled receptor molecules. The Examiner stated that "neither the specification nor the art of record disclose any disorders that can be effected by interfering with the activity using the EBI-2 receptor or fragments thereof." (Paper No. 8, page 12, lines 14-16.) However, the specification states that the antagonists of the G-protein coupled receptor may be used to treat, *inter alia*, myocardial infarction. Additionally, the polynucleotides of the invention may be used for the detection of heart disease.

The specification also states that examples of inhibitors of the EBI-2 G-protein coupled receptor include antibodies, small molecules, and soluble forms of the receptor. (Original specification, page 23, third full paragraph; page 24, first full paragraph and second full paragraph). The use of these EBI-2 G-protein coupled receptor molecules to

treat, for example, myocardial infarction is a specific use that is not generally applicable to all G-protein coupled receptors, much less to all proteins. *(See, e.g., Revised Interim Utility Guidelines Training Materials* ("*Utility Training Materials*") example 4, pages 32-33 (the use of an uncharacterized protein as an amino acid source or a protein supplement are uses that apply to "virtually every member of a general class of materials such as proteins" and therefore are not specific utilities under the facts of example 4.)). Thus, Applicants submit that the specification discloses at least one specific utility for the EBI-2 G-protein coupled receptor.

III. At Least One Asserted, Specific Utility Is Substantial.

The Examiner stated that "neither the specification nor the art of record disclose any activities or properties that would constitute 'real world' context for use for the claimed EBI-2 receptor and fragments thereof." (Paper No. 8, page 13.) Applicants respectfully disagree.

Applicants respectfully emphasize that the specification discloses at least one specific and substantial utility for the EBI-2 G-protein coupled receptor. A substantial utility is one that defines a "real world" use. (*Utility Training Materials* at page 6.) The use of EBI-2 G-protein coupled receptor molecules to produce antibodies, to treat, for example, myocardial infarction, or to detect heart disease are substantial utilities as they provide benefits to the public. Thus, at least one asserted use for the EBI-2 G-protein coupled receptor is specific and substantial, as well as credible, as discussed further below.

Real-world value of an invention requires that "one skilled in the art can use a

claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881, 883 (CCPA 1980). Furthermore, "any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a specific utility" (MPEP page 2107, column 2, lines 16-20). The specification and the claims provide support for the use of EBI-2 polynucleotides as a diagnostic for detecting the expression of EBI-2 (Specification page 27, third full paragraph). Indeed, as shown in the Hollopeter article discussed below and attached herewith, differential EBI-2 expression may indicate a perturbation in platelet aggregation, which can lead to myocardial infarction. Therefore, the use of EBI-2 GPCR as a diagnostic for heart disease provides a public benefit and has real world value. The detection of heart disease and/or treatment of myocardial infarction are substantial uses.

Applicants assert that the claimed invention is supported by a specific and substantial utility.

IV. At Least One Asserted, Specific And Substantial Utility Is Credible.

Although the Examiner has failed to carry the burden of showing that the disclosed utilities are unbelievable, Applicants submit herewith documentary evidence that the noted utilities of EBI-2 have been demonstrated in the art.

The Federal Circuit has set forth the standard by which an asserted utility is established through supporting data. The Federal Circuit pointed out that its "predecessor court has noted that adequate proof of any pharmacological activity constitutes a showing of practical utility." *Cross v. Izuka,* 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985),

citing Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881 (C.C.P.A. 1980) and *Rey-Bellet v. Englehardt* 493 F.2d 1380, 181 U.S.P.Q. 453 (C.C.P.A. 1974). Specifically, the Federal Circuit held:

> [B]ased upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of a pharmacological activity is reasonably based upon the probative evidence.

Cross v. Izuka, 753 F.3d at 1050.

Furthermore, utility can exist for therapeutic inventions "despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition." MPEP § 2107 (III) at 2100-27. "Usefulness in patent law . . . necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." *In re Brana,* 51 F.3d at 1568.

There is clearly a direct nexus between the G-protein coupled receptor (EBI-2) and heart disease, specifically myocardial infarction. The Examiner's attention is respectfully drawn to a post-filing date publication by others that have implicated EBI-2 in platelet aggregation. *See* Hollopeter, G. *et al.,Nature 409(6817)*:202-7 (2001). Hollopeter *et al.* reports the cloning of P2Y12, a G-protein coupled receptor which has an amino acid sequence identical to EBI-2. Moreover, just as the original specification states, e.g., at page 22, lines 29-32, the authors of this publication indicate that perturbations in this P2Y12/EBI-2 receptor-mediated activity can lead to cardiovascular diseases, including myocardial infarction. Thus, this publication by others confirms the

nexus between EBI-2 and the treatment and/or detection of heart disease.

The disclosure in Hollopeter *et al.* confirms the credibility of using EBI-2 polynucleotides to detect EBI-2 expression in heart disease conditions. (*See* original specification, page 8, line 19, page 15, third full paragraph, paragraph spanning pages 22-23). Therefore, the documentary evidence cited above confirms the credibility, as well as the specificity and substantiality, of at least one asserted utility for the EBI-2 polynucleotides of the present application.

In view of the facts set out above, Applicants submit that a skilled artisan would not reasonably doubt that the claimed polynucleotides can be useful in making EBI-2 proteins, generating antibodies, or diagnosing and/or treating heart diseases. As such, Applicants assert that the presently claimed invention possesses a credible, specific and substantial utility that constitutes a patentable utility under 35 U.S.C. § 101. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be reconsidered and withdrawn.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 23-29, 31, 33-39, 41, 43-51, 53, 55-64, 66, 68-77, 79, 81-89, 91, 93-97 and 99 were rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. (Paper No. 8.)

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific, substantial and credible asserted utility. The Examiner "should not impose a 35 U.S.C. 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. 101 rejection is proper." M.P.E.P. § 2107 (IV) at 2100-28. Therefore, because the claimed invention complies with the

utility requirement of 35 U.S.C. § 101, the rejections under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be withdrawn.

Claims 23-29, 31, 33-39, 41, 43-51, 53, 55-64, 66, 68-77, 79, 81-89, 91, 93-97 and 99 were rejected under 35 U.S.C. § 112, first paragraph for alleged lack of written description. (Paper No. 8.) Applicants respectfully traverse.

The written description requirement serves to ensure that the inventor had possession, as of the filing date, of the claimed subject matter. However, "how the specification accomplishes this is not material." *In re Wertheim*, 191 U.S.P.Q. 90, 96 (C.C.P.A. 1976). In *Regents of the University of California v. Eli Lilly & Co.*, the court stated, "[a] description of a genus of cDNAs may be achieved by means of [1] a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus ***or*** [2] a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Regents of the University of California v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997) (emphasis added), *cert. denied*, 66 U.S.L.W. 3688 (1998). Thus, the Federal Circuit has indicated that the written description requirement for generic claims directed to genetic material may be satisfied by providing the sequences of a representative number of members which fall within the scope of the genus ***or*** by providing a recitation of common structural features of the members of the genus.

Additionally, according to the court in *Eli Lilly & Co.*:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can *distinguish* such a formula from others and can *identify* many of the species that the claims encompass. *Accordingly, such a formula is*

normally an adequate description of the claimed genus.

Eli Lilly & Co. at 1406 (emphasis added).

Applicants submit that the present claims recite generic formulae that indicate with specificity the subject matter that the claims encompass. One of ordinary skill in the art can *distinguish* the present generic polynucleotides from others and can *identify* many of the species encompassed by the present claims. Accordingly, the present claim recitations are "*adequate description[s] of the claimed genus.*" *Id.* (emphasis added).

Additionally, for the reasons stated below, Applicants assert that the reference polynucleotide and polypeptide are representative of the claimed genus in satisfaction of the first test set forth in *Eli Lilly & Co.* Applicants also assert that the recitation of the complete sequence of the reference polynucleotide and encoded polypeptide constitutes a recitation of the structural features common to the members of the genus, in satisfaction of the second test. Concerning the first test, Applicants assert that the reference nucleic acid sequence (e.g., independent claims 23, 33, 43, 55, 68, 81, and 93) which falls within the scope of its respective genus, is representative of the genuses of polynucleotides encompassed by the claims. For example, polynucleotides at least 90% identical to the specific polynucleotide sequence will show activity, such as hybridization activity, much like the specific polynucleotide itself. Thus, polynucleotides comprising the specific sequences are exemplary of the structure of the variants within the genuses.

Concerning the second test, Applicants assert that the recitation of the *complete* EBI-2 G-protein coupled receptor polynucleotide sequence is a recitation of the structural features common to the members of its respective genus because the polynucleotides in the genus have at least 90% of their nucleic acid sequence (i.e., primary structure) in common with the

reference polynucleotide. Likewise, the recitation of the *complete* sequence of the EBI-2 G-protein coupled receptor polypeptide is a recitation of the structural features common to the members of its respective genus because the polynucleotides in the genus encode polypeptides having at least 90% of their amino acid sequence (i.e., primary structure) in common with the reference polypeptide as recited in claim 68.

The claims are also adequately described under the PTO's guidelines and *Synopsis of Application of Written Description Guidelines*. According to the guidelines:

> [t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by . . . disclosure of relevant, identifying characteristics, *i.e.*, [1] structure or other physical and/or chemical properties, [2] by functional characteristics . . . ***or*** [3] by a combination of such identifying characteristics.

Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶1, *"Written Description" Requirement*, 66 Fed. Reg. 1104, 1106 (Jan. 5, 2001) ("*Written Description Guidelines*") (emphasis added).

Thus, the guidelines indicate that a representative species may be adequately described through its structure, through its functional characteristics, ***or*** through a combination of its structure and function.

As discussed above, each member of each genus is described by reference to its sequence, i.e., its structure. The members of claim 23, for example, each shares at least 90% of its polynucleotide residues with 150 contiguous nucleotides of SEQ ID NO:1. Indeed, because of the degeneracy of the genetic code, a number of the polynucleotides within the scope of claim 23 encode a polypeptide that shares 100% of its amino acid residues with the reference polypeptide. Each member of the claimed genuses shares substantial sequence

identity with the relevant reference sequence. Thus, there is *not* substantial variation within each genus. The reference polynucleotide species is, therefore, representative of the respective genus and the description of the complete sequence for the representative species is an adequate written description for the genus encompassed by the claims.

Once the skilled artisan had the DNA and amino acid sequence of a given G-protein coupled receptor, the artisan could easily locate the extracellular, intracellular and transmembrane domains for that G-protein coupled receptor and identify many functionally important amino acid residues. In addition, the specification specifically discloses assays that can be utilized for identifying and isolating polynucleotides that encode these polypeptides. (See specification, page 11, lines 16-30 and page 15, lines 10-17.) Accordingly, Applicants submit that one skilled in the art would not have to engage in an undue amount of experimentation to make and use the claimed invention.

Further, one of ordinary skill in the art can readily envisage polynucleotides comprising SEQ ID NO:1 because such sequences can be combined with sequences known in the art such as vectors, regulatory regions, or marker sequences. (*See, e.g.,* original specification, paragraph spanning pages 15-16). Any substantial variability within the genuses would therefore arise due to elements that are not part of the inventors' contribution. Additionally, procedures for making variants having at least 90% identity were conventional in the art at the time of filing. Although there may be a degree of variability among the 90% identical variant species to which the claims are directed, the necessary common structural features remain, e.g., SEQ ID NO:1. Therefore, one skilled in the art would recognize that Applicants were in possession of the claimed genus.

For all of the above reasons, Applicants respectfully assert that the Examiner has

failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Thus, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph under both tests set out in *Eli Lilly & Co.* and under the PTO's *Written Description Guidelines* and *Synopsis*. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph - Deposit Rules

Claims 23-29, 31, 33-39, 41, 43-51, 53, 55-64, 66, 68-77, 79, 81-83, 84-89, 91, 94-97 and 99 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly being nonenabled for reciting deposited biological material. The Examiner required that the specification be amended to recite the address of the ATCC, and required that particular averments be made concerning the deposit.

Applicants have amended the specification accordingly. As amended, the specification discloses the address of the depository. "Statement Concerning the Deposited cDNA Clone" which contains the necessary averments will be submitted upon receipt by the undersigned. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant(s) therefore respectfully request(s) that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant(s) believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

In the Specification:

The sentence beginning at page 1, line 1:

This Application is a continuation of U.S. Application No. 08/852,824 filed May 7, 1997, now U.S. Patent No. 6,060,272, issued May 9, 2000, the disclosure of which is incorporated herein by reference in its entirety.

The paragraph beginning on page 7, line 17:

In accordance with an aspect of the present invention, there is provided an isolated nucleic acid (polynucleotide) which encodes for the mature polypeptide having the deduced amino acid sequence of Figures 3A and 3B (SEQ ID NO:4) or for the mature polypeptide encoded by the cDNA of the clone deposited with the ATCC, 10801 University Boulevard, Manassas, VA 20110-2209, as ATCC Deposit No. 209004 on 4/28/97.

The paragraph beginning on page 10, line 21:

The present invention also includes polynucleotides, wherein the coding sequence for the mature polypeptide may be fused in the same reading frame to a polynucleotide sequence which aids in expression and secretion of a polypeptide from a host cell, for example, a leader sequence which functions as a secretory sequence for controlling

transport of a polypeptide from the cell. The polypeptide having a leader sequence is a preprotein and may have the leader sequence cleaved by the host cell to form the mature form of the polypeptide. The polynucleotides may also code for a proprotein which is the mature protein plus additional 5[1]' amino acid residues. A mature protein having a prosequence is a proprotein and is an inactive form of the protein. Once the prosequence is cleaved an active mature protein remains.

In the Claims:

Please cancel Claim 82.

35. (Once amended) The polynucleotide of claim 33, wherein said nucleic acid encodes a polypeptide which [has G-protein-coupled receptor activity.] binds an antibody having specificity for the polypeptide of SEQ ID NO:2.

47. (Once amended) The polynucleotide of claim 43, wherein said nucleic acid encodes a polypeptide which [has G protein-coupled receptor activity.] binds an antibody having specificity for the polypeptide of SEQ ID NO:2.

60. (Once amended) The polynucleotide of claim 55, wherein said nucleic acid encodes a polypeptide which [has G-protein coupled receptor activity.] binds an antibody having specificity for the polypeptide of SEQ ID NO:2.

73. (Once amended) The polynucleotide of claim 68, wherein said nucleic acid

encodes a polypeptide which [has G-protein coupled receptor activity.] binds an antibody having specificity for the polypeptide of SEQ ID NO:2.

83. (Once amended) The polynucleotide of claim [82] 81, wherein said nucleic acid encodes a polypeptide which binds an antibody having specificity for the polypeptide of SEQ ID NO:2.